UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/663,082	09/16/2003	Nicholas Pullen	PC25214A	1683

28523 7590 02/15/2005

PFIZER INC.
PATENT DEPARTMENT, MS8260-1611
EASTERN POINT ROAD
GROTON, CT 06340

EXAMINER	
HENLEY III, RAYMOND J	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 02/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/663,082	PULLEN ET AL.	
	Examiner	Art Unit	
	Raymond J Henley III	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/5/04 & 9/16/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

CLAIMS 1-13 ARE PRESENTED FOR EXAMINATION

Applicants' Information Disclosure Statements filed September 16, 2003 and February 5, 2004 have been received and entered into the application. As reflected by the attached, completed copies of form "PTO-FB-A820", the Examiner has considered the cited references.

Claims Renumbered

A claim numbered as "2" was not present in the claims as originally filed. Accordingly, pursuant to 37 C.F.R. § 1.126, claims 3-14 as originally filed have been renumbered as 2-13, respectively. References to claims herein are made consistent with this new numbering. Applicants need to adopt such numbering in any future correspondence with the Office.

Claim Rejection - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

"The primary purpose of this requirement of definiteness of claim language is to ensure that the scope of the claims is clear so the public is informed of the boundaries of what constitutes infringement of the patent. A secondary purpose is to provide a clear measure of what applicants regard as the invention so that it can be determined whether the claimed invention meets all the criteria for patentability and whether the specification meets the criteria of 35 U.S.C. 112, first paragraph with respect to the claimed invention." (See MPEP § 2173).

The term "derivative" in the expression "a pharmaceutically acceptable derivative thereof", as recited in claims 1-12, is a relative term which renders the claim indefinite. In particular, "derivative" does not particularly point out the degree or type of derivation that a given compound may have in relation to the parent compound and still be considered a "derivative" as intended by Applicants. Applicants have failed to provide any definition for this term in the present specification. Lacking a clear meaning of the term "derivative", the skilled artisan would not be reasonably apprised of the metes and bounds of the subject matter for which Applicants seek patent protection and the identity of those compounds that are intended to be included or excluded by the term "derivative" would be open to subjective interpretation. Such interpretation is inconsistent with the tenor and express requirements of 35 U.S.C. § 112, second paragraph and thus the claims are deemed properly rejected.

Legal Standard for Anticipation/Inherency Under - 35 USC § 102

To anticipate a claim under 35 U.S.C. § 102, a single prior art reference must place the invention in the public's possession by disclosing each and every element of the claimed invention in a manner sufficient to enable one skilled in the art to practice the invention. *Scripps Clinic & Research Foundation v. Genetech, Inc.,* 927 F.2d 1565, 1576, 18 U.S.P.Q.2d 1001, 1001 (Fed. Cir. 1991); *In re Donahue,* 766 F2d531, 533, 226 U.S.P.Q. 619, 621 (Fed. Cir. 1985). To anticipate, the prior art must either expressly or inherently disclose every limitation of the claimed invention. *MEHL/Biophile Int'l Corp. v. Milgraum,* 192 F.3d 1362, 1365, 52 U.S.P.Q.2d 1303, 1303 (Fed. Cir. 1999) (citing to *In re Schreiber,* 128 F.3d 1473, 1477, 44 U.S.P.Q. 1429, 1431 (Fed. Cir. 1997)); *Atlas Powder Co. v. Ireco Inc.,* 190 F.3d 1342, 1347, 51

U.S.P.Q.2d 1943, 1946 (Fed. Cir. 1999). To inherently anticipate, the prior art must necessarily function in accordance with, or include, the claimed limitations. *MEHL/Biophile*, 192 F.3d at 1365, 52 U.S.P.Q.2d at 1303. However, it is not required that those of ordinary skill in the art recognize the inherent characteristics or the function of the prior art. *Id.* Specifically, discovery of the mechanism underlying a known process does not make it patentable.

Claim Rejection - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 7, 10 and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Scott (WO 99/11260, cited by Applicants) who teach pharmaceutical compositions which comprise an effective amount of atorvastatin or a pharmaceutically acceptable salt, hydrate or solvate i.e., a derivative, thereof (page 6, lines 2-5 and page 15, lines 10-23) and an effective amount of an antihypertensive agent which may be an alpha-adrenergic receptor blocker or a pharmaceutically acceptable salt, hydrate or solvate i.e. derivative, thereof, (page 6, lines 6-7 and page 15, lines 10-23), such as doxazosin (page 8, line 21), prazocin (page 8, line 22), naftopidil (page 20, line 21), and tamsulosin (page 20, line 24). The components of the compositions are further taught to be present in the compositions either individually or in combination, i.e., see the requirement of present claims 10 and 12 "for simultaneous, sequential or separate administration" (page 37, lines 18-22).

Scott fails to expressly disclose that the compositions are useful for the treatment of benign prostatic hypertrophy, (a.k.a. BPH). Here, however, the statement in the claims that the compositions are intended for use in the treatment of BPH does not impart any physical or otherwise material feature to the composition that is not present in the compositions of the reference and thus is not treated as a claim limitation. Any terminology in the preamble that limits the structure of the claimed invention must be treated as a claim limitation. See, e.g., *Corning Glass Works v. Sumitomo Elec. U.S.A., Inc.*, 868 F.2d 1251, 1257, 9 USPQ2d 1962, 1966 (Fed. Cir. 1989). Also "[t]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer.". See *Atlas Powder Co. v. Ireco Inc.*, 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999).

Claim Rejection - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

I Claims 8, 9, 11 and 12 rejected under 35 U.S.C. 103(a) as being unpatentable over Scott (WO 99/11260), as relied on above, in view of Davis et al. (U.S. Patent Application Publication No. 2003/0133978, cited by the Examiner) and Blagg et al., (U.S. Patent Application No. 2004/0029859, cited by the Examiner).

The difference between the above and the claimed subject matter lies in that Scott fails to expressly disclose that either (i) 4-amino-6,7-dimethoxy-2-(5-methanesulfonamido-1,2,3,4-tetrahydroisoquinol-2-yl)-5-(2-pyridyl)-quinazoline or a pharmaceutically acceptable derivative thereof or (ii) 5-cyclopropyl-7-methoxy-2-(2-morpholin-4-ylmethyl-7,8-dihydro[1,6]-naphthyridin-6(5H)-yl)-4(3H)-quinazolinone or a pharmaceutically acceptable derivative thereof may be the present in the composition in addition to the atorvastatin component.

However, the difference between the subject matter sought to be patented and the prior art is such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains because Scott indicates that, as a therapeutic class of active agents, alpha-adrenergic receptor blockers or a pharmaceutically acceptable salt, hydrate or solvate i.e. derivative, thereof, (page 6, lines 6-7; page 15, lines 10-23; and page 20, lines 13-29) may be employed while both (i) 4-amino-6,7-dimethoxy-2-(5-methanesulfonamido-1,2,3,4-tetrahydroisoquinol-2-yl)-5-(2-pyridyl)-quinazoline or a pharmaceutically acceptable derivative thereof and (ii) 5-cyclopropyl-7-methoxy-2-(2-morpholin-4-ylmethyl-7,8-dihydro[1,6]-naphthyridin-6(5H)-yl)-4(3H)-quinazolinone or a pharmaceutically acceptable derivative thereof were known to be alpha-

adrenergic receptor blockers (see Davis et al., U.S. Patent Application Publication No. 2003/0133978, at page 5, col. 1, paragraph [0064] and Blagg et al., U.S. Patent Application No. 2004/0029859, at the abstract and page 3, paragraph [0073]. The skilled artisan would have been motivated to employ the specific alpha-adrenergic receptor blockers of the secondary references in the compositions taught by Scott because Scott expressly discloses that alpha-adrenergic receptor blockers in general may be employed.

II Claims 1-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weisman et al. (U.S. Patent Application Publication No. 2002/0004521, cited by Applicants) and Thompson et al. (U.S. Patent No. 6,177,430, cited by the Examiner) in view of Scott (WO 99/11260), Lawyer (U.S. Patent No. 6,423,719, cited by the Examiner), Davis et al. (U.S. Patent Application Publication No. 2003/0133978) and Blagg et al., (U.S. Patent Application No. 2004/0029859, cited by the Examiner).

Weisman et al. teach a method for the treatment of BPH which comprises administering to a patient in need thereof, an effective amount of an HMG-CoA reductase inhibitor, such as the calcium salt of atorvastatin (see the abstract and page 1, col. 1, paragraphs [0004] and [0008]).

Thompson et al. teach a method for the treatment of BPH which comprises administering to a patient in need thereof, an effective amount of α_1-adrenoreceptor antagonist or a pharmaceutically acceptable salt thereof, such as alfuzosin, terazosin, bunazosin, doxazosin, prazocin and tamsulosin (see the abstract and col. 2, lines 42 – col. 3, line 6).

The differences between the above and the claimed subject matter lie in that neither of the above references teach (i) *a combination* of an HMG-CoA reductase inhibitor, such as atorvastatin, and an alpha adrenergic receptor antagonist for the treatment of BPH or (ii)

naftopidil, silodosin, 4-amino-6,7-dimethoxy-2-(5-methanesulfonamido-1,2,3,4-tetrahydroisoquinol-2-yl)-5-(2-pyridyl)-quinazoline or a pharmaceutically acceptable derivative thereof, or 5-cyclopropyl-7-methoxy-2-(2-morpholin-4-ylmethyl-7,8-dihydro[1,6]-naphthyridin-6(5H)-yl)-4(3H)-quinazolinone or a pharmaceutically acceptable derivative thereof as alpha adrenergic receptor antagonists.

However, the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains because:

(i) It has been held that it is considered prima facie obvious to have combined two or more ingredients each of which was known to be useful for the same purpose in order to form a third composition that is useful for the very same purpose. The idea for combining them flows logically from their have been used separately. See *In re Kerkhoven*, 205 U.S.P.Q. 1069 (CCPA 1980) and the cases cited therein. The skilled artisan would have been motivated to combine such ingredients in order to achieve *at least* additive results and to provide the individual being treated with the most convenient, effective therapy possible. Further, as evidenced by Lawyer, one of ordinary skill in the art was well aware that BPH could be effectively treated with combinations of active agents in which an alpha adrenergic receptor antagonist was employed as one of the active agents (see Lawyer at col. 1, lines 12-14 and col. 4, lines 1-27).

The Examiner has here relied upon legal precedent as the source of supporting rationale for the conclusion that the presently claimed subject matter would have been obvious. Such a rationale is proper and is provided for in MPEP § 2144.04.

(ii) Thompson et al. teach alpha adrenergic receptor antagonist may be used in general, i.e., they do not limit their teachings to the specifically name alpha adrenergic receptor antagonists, i.e., "[*p*]*referably*, the α_1-adrenoreceptor antagonists are selected from..." (col. 2, lines 51-57) and "α_1-Adrenoreceptor antagonists useful in the practice of the invention *include*..." (col. 2, line 64 – col. 3, line 6) while naftopidil, silodosin, 4-amino-6,7-dimethoxy-2-(5-methanesulfonamido-1,2,3,4-tetrahydroisoquinol-2-yl)-5-(2-pyridyl)-quinazoline or a pharmaceutically acceptable derivative thereof, and 5-cyclopropyl-7-methoxy-2-(2-morpholin-4-ylmethyl-7,8-dihydro[1,6]-naphthyridin-6(5H)-yl)-4(3H)-quinazolinone or a pharmaceutically acceptable derivative thereof were each well known to one of ordinary skill in the art as alpha adrenergic receptor antagonists (see Scott, WO 99/11260 at page 20, line 21 "naftopidil"; Davis et al., U.S. Patent Application No. 2003/0133978, at page 5, col. 1, lines 1-3 "4-amino-6,7-dimethoxy-2-(5-methanesulfonamido-1,2,3,4-tetrahydroisoquinol-2-yl)-5-(2-pyridyl)-quinazoline, and its pharmaceutically acceptable salts" and line 4 thereof "silodosin"; and Blagg et al., U.S. Patent Application No. 2004/0029859, the abstract and page 3, paragraph [0073], "5-cyclopropyl-7-methoxy-2-(2-morpholin-4-ylmethyl-7,8-dihydro[1,6]-naphthyridin-6(5H)-yl)-4(3H)-quinazolinone").

The skilled artisan would have been motivated to employ the specific alpha-adrenergic receptor blockers of the secondary references in the methods taught and/or suggested by the primary references because, as noted above, Thompson et al. expressly discloses that alpha-adrenergic receptor blockers in general may be employed.

For the above reasons, the claims are deemed properly rejected and none are allowed.

The references cited on the attached form PTO-892 and not relied on are included to show the general state of the art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Raymond J Henley III whose telephone number is 571-272-0575. The examiner can normally be reached on M-F, 8:30 am to 4:00 pm Eastern Time.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Raymond J Henley III
Primary Examiner
Art Unit 1614

February 12, 2005